

Claims:

1. Nucleic acid encoding an amino acid sequence variant of an adhesion.
- 5 2. The nucleic acid of claim 1 wherein the adhesion is a CD4 polypeptide.
3. The nucleic acid of claim 2 wherein the variant is a CD4 polypeptide in which nucleic acid encoding the transmembrane domain has been modified whereby the CD4 polypeptide encoded
10 thereby contains an inactivated transmembrane domain.
4. The nucleic acid of claim 3 wherein the transmembrane domain has been inactivated by its deletion or by substituting for the transmembrane domain an amino acid sequence having a
15 substantially hydrophilic hydropathy profile.
5. The nucleic acid of claim 2 wherein the variant comprises a fusion of (a) a polypeptide different from the CD4 and (b) a CD4 polypeptide.
20
6. The nucleic acid of claim 5 wherein the polypeptide different from the CD4 bears a non-CD4 immune epitope.
- 25 7. The nucleic acid of claim 6 wherein the polypeptide different from CD4 is fused to the amino or carboxyl terminus of mature CD4 and the transmembrane domain of CD4 has been inactivated.
8. The nucleic acid of claim 5 wherein the different polypeptide comprises a signal sequence.
30
9. The nucleic acid of claim 5 wherein the different polypeptide contains about from 5 to 1000 residues.

35

10. The nucleic acid of claim 9 wherein the different polypeptide is capable of eliciting a humoral immune response in an animal.
- 5 11. The nucleic acid of claim 10 wherein the different polypeptide is a viral polypeptide or an allergen.
12. The nucleic acid of claim 5 wherein the different polypeptide is a human plasma protein having a plasma half life greater than from which the transmembrane domain has been deleted.
- 10 13. The nucleic acid of claim 12 wherein the variant is a fusion of a polypeptide comprising at least one V-like domain of CD4 fused with a polypeptide comprising an immunoglobulin constant domain.
- 15 14. The nucleic acid of claim 1 wherein the adheson is CD4, CD8 or the high affinity IgE receptor.
- 20 15. The nucleic acid of claim 2 wherein the variant consists essentially of the V₁ through V₄ or V₁ through V₂ regions of the CD4 antigen.
16. The nucleic acid of claim 2 which consists essentially of the CD4 insert of pCD4DN1a.
- 25 17. The nucleic acid of claim 12 wherein the different polypeptide is albumin, apolipoprotein or transferrin.
18. The nucleic acid of claim 8 wherein the signal sequence is a bacterial signal sequence.
- 30 19. The nucleic acid of claim 15 wherein the variant consists essentially of CD4 residues 1-368.

20. The nucleic acid of claim 15 wherein the variant consists essentially of CD4 residues 1-180.
- 5 21. The nucleic acid of claim 13 wherein the immunoglobulin constant domain is the constant domain of an IgG heavy chain.
22. The nucleic acid of claim 5 wherein the different polypeptide is a cytotoxic polypeptide.
- 10 23. The nucleic acid of claim 5 wherein the cytotoxic polypeptide is the diphtheria toxin A.
24. A composition comprising an adheson amino acid sequence variant which is incapable of cell membrane anchorage.
- 15 25. The composition of claim 24 wherein the adheson variant comprises a CD4 amino acid sequence capable of binding gp120.
- 20 26. The composition of claim 25 further comprising an agent for inhibiting the aggregation of the variant selected from the group of a predetermined protein and a surfactant.
27. The composition of claim 26 wherein the agent is a surfactant.
- 25 28. The composition of claim 27 wherein the surfactant is Tween 80 or Tween 20.
- 30 29. The composition of claim 25 wherein the CD4 transmembrane domain has been deleted or has been substituted for by an amino acid sequence having a substantially hydrophilic hydropathy profile.

30. The composition of claim 29 which is sterile and which further comprises a physiologically acceptable carrier.
- 5 31. The composition of claim 25 wherein the variant comprises an immunoglobulin amino acid sequence.
32. The composition of claim 31 wherein the immunoglobulin sequence comprises a constant domain sequence of an immunoglobulin heavy chain.
- 10 33. The composition of claim 32 wherein the constant domain is linked at its N-terminus to the C-terminus of a transmembrane-deleted CD4 polypeptide.
- 15 34. The composition of claim 33 wherein the CD4 polypeptide contains V_1V_2 .
35. The composition of claim 33 wherein the CD4 polypeptide contains $V_1V_2V_3V_4$.
- 20 36. The composition of claim 31 wherein the the variant is in the form of a dimer.
- 25 37. The composition of claim 36 wherein the composition comprises a fusion of a CD4 V-like domain to an immunoglobulin heavy chain constant domain.

38. The composition of claim 31 wherein the variant is selected from the group consisting of
- (a) AC_L ;
 - (b) AC_L-AC_L ;
 - 5 (c) $AC_H-[AC_H, AC_L-AC_H, AC_L-V_HC_H, V_LC_L-AC_H, \text{ or } V_LC_L-V_HC_H]$;
 - (d) $AC_L-AC_H-[AC_H, AC_L-AC_H, AC_L-V_HC_H, V_LC_L-AC_H, \text{ or } V_LC_L-V_HC_H]$;
 - (e) $AC_L-V_HC_H-[AC_H, AC_L-AC_H, AC_L-V_HC_H, V_LC_L-AC_H, \text{ or } V_LC_L-V_HC_H]$;
 - (f) $V_LC_L-AC_H-[AC_H, AC_L-AC_H, AC_L-V_HC_H, V_LC_L-AC_H, \text{ or } V_LC_L-V_HC_H]$; or
 - (g) $[A-Y]_n-[V_LC_L-V_HC_H]_2$
- 10 wherein A is a CD4 polypeptide containing a CD4 variable region-like domain; V_L , V_H , C_L and C_H represent light or heavy chain variable or constant domains of an immunoglobulin; n is an integer; and Y designates the residue of a covalent cross-linking agent.
- 15
39. The composition of claim 38 wherein the V_L and V_H domains are capable of binding a predetermined antigen.
40. The composition of claim 31 wherein the immunoglobulin sequence
- 20 is obtained from IgG1, IgG2, IgG3, IgG4, IgA, IgE, IgD or IgM.
41. The composition of claim 25 wherein the variant comprises a polypeptide different from CD4 which is nonimmunogenic in humans.
- 25
42. The composition of claim 41 wherein the variant comprises a polypeptide which is immunogenic in humans.
43. The composition of claim 41 wherein the variant comprises a
- 30 polypeptide having a human plasma half life which is greater than about 20 hours.
44. The composition of claim 41 wherein the variant comprises a human transferrin, apolipoprotein or albumin polypeptide.
- 35
45. The composition of claim 25 wherein the variant comprises a cytotoxic polypeptide.
46. The composition of claim 45 wherein the cytotoxic polypeptide is
- 40 ricin A chain or diphtheria toxin A.

- 5 47. A polypeptide comprising a CD4 amino acid sequence capable of binding gp120 which is cross-linked to (a) polypeptide having a plasma half life of greater than about 20 hours or (b) a cytotoxic polypeptide.
48. The polypeptide of claim 47 wherein the polypeptide of (a) is transferrin, an apolipoprotein or albumin.
- 10 49. The polypeptide of claim 47 wherein the cytotoxic polypeptide is cross-linked to the CD4 variable-like domain by a bifunctional cross-linking agent.
- 15 50. A method for preparing an adhesion variant comprising transfecting a host cell with the nucleic acid of claim 1.
51. A method for preparing an adhesion variant comprising recovering the variant from the culture of a host cell transfected with the nucleic acid of claim 1.
- 20 52. The method of claim 51 wherein the adhesion is CD4 and the variant is recovered from the culture medium of the host cell or from the cell itself.
- 25 53. The method of claim 52 wherein the variant is recovered by adsorption onto a cation exchange resin.
54. The method of claim 53 wherein the variant is recovered by adsorption of contaminants onto an anion exchange resin.
- 30 55. The method of claim 52 wherein the variant lacks a functional transmembrane domain.
- 35 56. The method of claim 52 wherein wherein a salt is added to the culture medium to occupy charged domains of the variant, the resulting solution is contacted with a hydrophobic affinity chromatography resin to adsorb the variant, and the variant eluted from the resin by washing the resin with a declining gradient of salt.
- 40 57. The method of claim 52 wherein the variant is recovered by

immunoaffinity chromatography.

5 58. The method of claim 57 wherein the immunoaffinity chromatography is directed against a polypeptide different from CD4 which is fused to CD4.

59. A method for the treatment of an HIV infection comprising administering to a patient infected with HIV a therapeutically effective dose of an amino acid sequence variant of CD4.

10

60. A replicable vector comprising the nucleic acid of claim 1.